WO 99/58679

09/674716

PCT/GB99/01434


```
          AAGCTTTACAGTTACTCAGCACACAGGACCTCACCATGGATTTTGGGCTGATTTTTTTTA
        1 ---------+---------+---------+---------+---------+---------+  60
          TTCGAAATGTCAATGAGTCGTGTGTCCTGGAGTGGTACCTAAAACCCGACTAAAAAAAAT
C           A  L  Q  L  L  S  T  Q  D  L  T  M  D  F  G  L  I  F  F  I  -

          TTGTTCTTTTAAAAGGGGTCCAGAGTGAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGG
       61 ---------+---------+---------+---------+---------+---------+ 120
          AACAAGAAAATTTTCCCCAGGTCTCACTTCACTTCGAACTCCTCAGACCTCCTCCGAACC
C           V  L  L  K  G  V  Q  S  E  V  K  L  E  E  S  G  G  G  L  V  -

          TGCAACCTGGAGGATCCATGAAACTCTCCTGTGTAGCCTCTGGATTTACTTTCAGTGGCT
      121 ---------+---------+---------+---------+---------+---------+ 180
          ACGTTGGACCTCCTAGGTACTTTGAGAGGACACATCGGAGACCTAAATGAAAGTCACCGA
C           Q  P  G  G  S  M  K  L  S  C  V  A  S  G  F  T  F  S  G  Y  -

          ACTGGATGTCTTGGGTCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTA
      181 ---------+---------+---------+---------+---------+---------+ 240
          TGACCTACAGAACCCAGGCGGTCAGAGGTCTCTTCCCCGAACTCACCCAACGACTTTAAT
C           W  M  S  W  V  R  Q  S  P  E  K  G  L  E  W  V  A  E  I  R  -

          GATTGAAATCTGATAATTATGCAACACATTATGCGGAGTCTGTGAAAGGGAAGTTCACCA
      241 ---------+---------+---------+---------+---------+---------+ 300
          CTAACTTTAGACTATTAATACGTTGTGTAATACGCCTCAGACACTTTCCCTTCAAGTGGT
C           L  K  S  D  N  Y  A  T  H  Y  A  E  S  V  K  G  K  F  T  I  -

          TCTCAAGAGATGATTCCAAAAGTCGTCTCTACCTGCAAATGAACAGCTTAAGAGCTGAAG
      301 ---------+---------+---------+---------+---------+---------+ 360
          AGAGTTCTCTACTAAGGTTTTCAGCAGAGATGGACGTTTACTTGTCGAATTCTCGACTTC
C           S  R  D  D  S  K  S  R  L  Y  L  Q  M  N  S  L  R  A  E  D  -

          ACAGTGGAGTTTATTACTGTACAGATTTCATAGACTGGGGCCAAGGGACACTAGT
      361 ---------+---------+---------+---------+---------+----- 415
          TGTCACCTCAAATAATGACATGTCTAAAGTATCTGACCCCGGTTCCCTGTGATCA
C           S  G  V  Y  Y  C  T  D  F  I  D  W  G  Q  G  T  L     -
```

FIG. 1

```
                AAGCTTTACAGTTACTCAGCACACAGGACCTCACCATGAGGTTCTCTGTTCAGTTTCTGG
      1 ---------+---------+---------+---------+---------+---------+---------+ 60
                TTCGAAATGTCAATGAGTCGTGTGTCCTGGAGTGGTACTCCAAGAGACAAGTCAAAGACC
C               A   L   Q   L   L   S   T   Q   D   L   T   M   R   F   S   V   Q   F   L   G  -

                GGGTGCTTATGTTCTGGATCTCTGGAGTCAGTGGGGATATTGTGATAACCCAGGATGAAC
     61 ---------+---------+---------+---------+---------+---------+---------+ 120
                CCCACGAATACAAGACCTAGAGACCTCAGTCACCCCTATAACACTATTGGGTCCTACTTG
C               V   L   M   F   W   I   S   G   V   S   G   D   I   V   I   T   Q   D   E   L  -

                TCTCCAATCCTGTCACTTCTGGAGAATCAGTTTCCATCTCCTGCAGGTCTAGTAAGAGTC
    121 ---------+---------+---------+---------+---------+---------+---------+ 180
                AGAGGTTAGGACAGTGAAGACCTCTTAGTCAAAGGTAGAGGACGTCCAGATCATTCTCAG
C               S   N   P   V   T   S   G   E   S   V   S   I   S   C   R   S   S   K   S   L  -

                TCCTGTATAAGGATGGGAAGACATACTTGAATTGGTTTCTGCAGAGACCAGGACAATCTC
    181 ---------+---------+---------+---------+---------+---------+---------+ 240
                AGGACATATTCCTACCCTTCTGTATGAACTTAACCAAAGACGTCTCTGGTCCTGTTAGAG
C               L   Y   K   D   G   K   T   Y   L   N   W   F   L   Q   R   P   G   Q   S   P  -

                CTCAGCTCCTGATGTATTTGATGTCCACCCGTGCATCAGGAGTCTCAGACCGGTTTAGTG
    241 ---------+---------+---------+---------+---------+---------+---------+ 300
                GAGTCGAGGACTACATAAACTACAGGTGGGCACGTAGTCCTCAGAGTCTGGCCAAATCAC
C               Q   L   L   M   Y   L   M   S   T   R   A   S   G   V   S   D   R   F   S   G  -

                GCAGTGGGTCAGGCACAGATTTCACCCTGGAAATCAGTAGAGTGAAGGCTGAGGATGTGG
    301 ---------+---------+---------+---------+---------+---------+---------+ 360
                CGTCACCCAGTCCGTGTCTAAAGTGGGACCTTTAGTCATCTCACTTCCGACTCCTACACC
C               S   G   S   G   T   D   F   T   L   E   I   S   R   V   K   A   E   D   V   G  -

                GTGTGTATTACTGTCAACAACTTGTAGAGTATCCATTCACGTTCGGCTCGGGGACAAAGT
    361 ---------+---------+---------+---------+---------+---------+---------+ 420
                CACACATAATGACAGTTGTTGAACATCTCATAGGTAAGTGCAAGCCGAGCCCCTGTTTCA
C               V   Y   Y   C   Q   Q   L   V   E   Y   P   F   T   F   G   S   G   T   K   L  -

                TGGAAATAAAACGTACG
    421 ----------------- 437
                ACCTTTATTTTGCATGC
C               E   I   K   R   T  -
```

FIG. 2

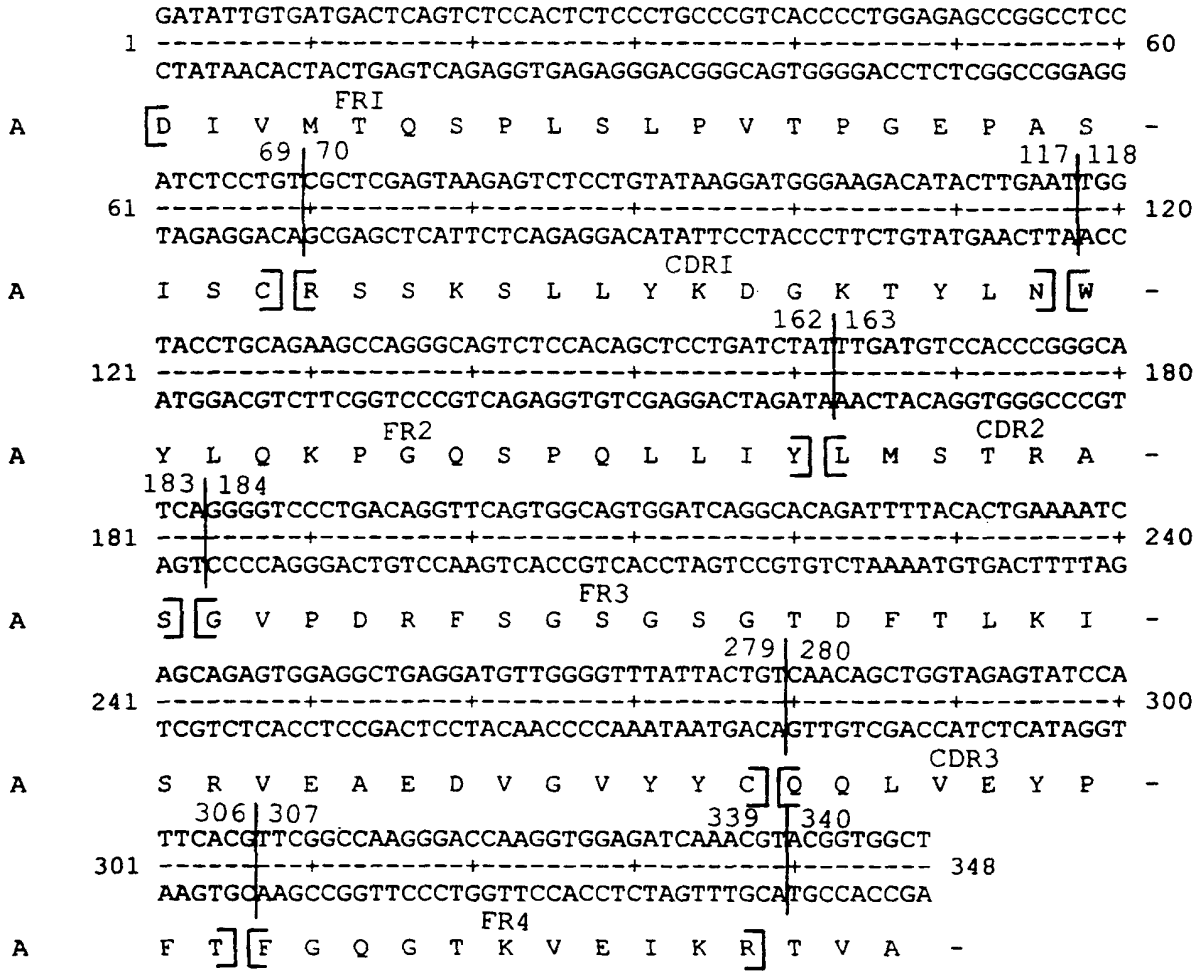
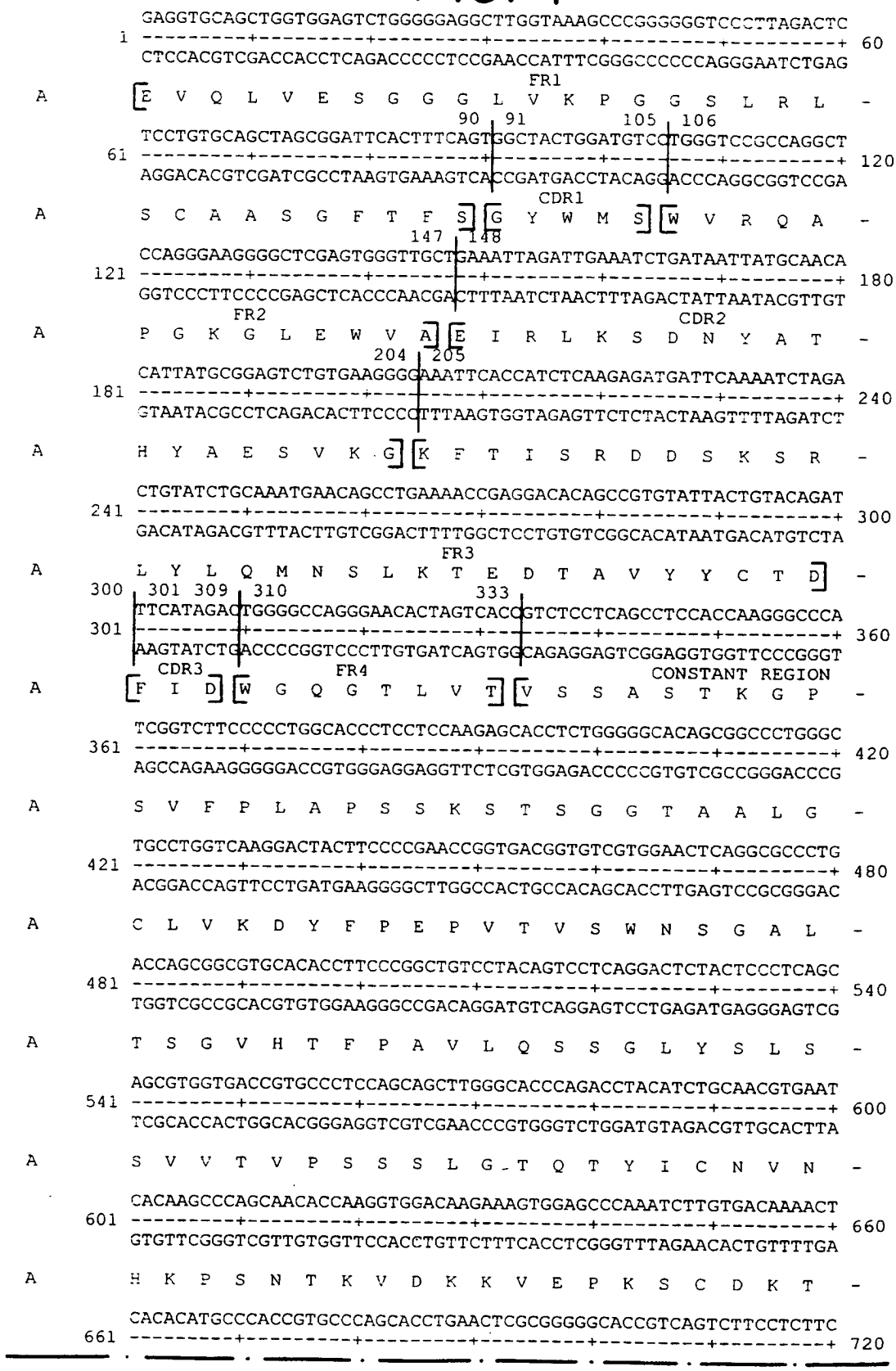

GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCC
1
CTATAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGGGGACCTCTCGGCCGGAGG
FRI
A D I V M T Q S P L S L P V T P G E P A S -
69 70
117 118
ATCTCCTGTCGCTCGAGTAAGAGTCTCCTGTATAAGGATGGGAAGACATACTTGAATTGG
61
120
TAGAGGACAGCGAGCTCATTCTCAGAGGACATATTCCTACCCTTCTGTATGAACTTAACC
CDRI
A I S C R S S K S L L Y K D G K T Y L N W -
162 163
TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTATTTGATGTCCACCCGGGCA
121
180
ATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATAAACTACAGGTGGGCCCGT
FR2
CDR2
A Y L Q K P G Q S P Q L L I Y L M S T R A -
183 184
TCAGGGGTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACAGATTTTACACTGAAAATC
181
240
AGTCCCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGTCTAAAATGTGACTTTTAG
FR3
A S G V P D R F S G S G S G T D F T L K I -
279 280
AGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGTCAACAGCTGGTAGAGTATCCA
241
300
TCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACAGTTGTCGACCATCTCATAGGT
CDR3
A S R V E A E D V G V Y Y C Q Q L V E Y P -
306 307
339 340
TTCACGTTCGGCCAAGGGACCAAGGTGGAGATCAAACGTACGGTGGCT
301
348
AAGTGCAAGCCGGTTCCCTGGTTCCACCTCTAGTTTGCATGCCACCGA
FR4
A F T F G Q G T K V E I K R T V A -

FIG. 3

FIG. 4



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                GTGTGTACGGGTGGCACGGGTCGTGGACTTGAGCGCCCCCGTGGCAGTCAGAAGGAGAAG

A               H  T  C  P  P  C  P  A  P  E  L  A  G  A  P  S  V  F  L  F  -

                CCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTG
          721   ---------+---------+---------+---------+---------+---------+  780
                GGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCAC

A               P  P  K  P  K  D  T  L  M  I  S  R  T  P  E  V  T  C  V  V  -

                GTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG
          781   ---------+---------+---------+---------+---------+---------+  840
                CACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTC

A               V  D  V  S  H  E  D  P  E  V  K  F  N  W  Y  V  D  G  V  E  -

                GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
          841   ---------+---------+---------+---------+---------+---------+  900
                CACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAG

A               V  H  N  A  K  T  K  P  R  E  E  Q  Y  N  S  T  Y  R  V  V  -

                AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTC
          901   ---------+---------+---------+---------+---------+---------+  960
                TCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAG

A               S  V  L  T  V  L  H  Q  D  W  L  N  G  K  E  Y  K  C  K  V  -

                TCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCC
          961   ---------+---------+---------+---------+---------+---------+  1020
                AGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGG

A               S  N  K  A  L  P  A  P  I  E  K  T  I  S  K  A  K  G  Q  P  -

                CGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTC
         1021   ---------+---------+---------+---------+---------+---------+  1080
                GCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAG

A               R  E  P  Q  V  Y  T  L  P  P  S  R  D  E  L  T  K  N  Q  V  -

                AGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC
         1081   ---------+---------+---------+---------+---------+---------+  1140
                TCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCG

A               S  L  T  C  L  V  K  G  F  Y  P  S  D  I  A  V  E  W  E  S  -

                AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCC
         1141   ---------+---------+---------+---------+---------+---------+  1200
                TTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGG

A               N  G  Q  P  E  N  N  Y  K  T  T  P  P  V  L  D  S  D  G  S  -

                TTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTC
         1201   ---------+---------+---------+---------+---------+---------+  1260
                AAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAG

A               F  F  L  Y  S  K  L  T  V  D  K  S  R  W  Q  Q  G  N  V  F  -

                TCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTG
         1261   ---------+---------+---------+---------+---------+---------+  1320
                AGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGAC

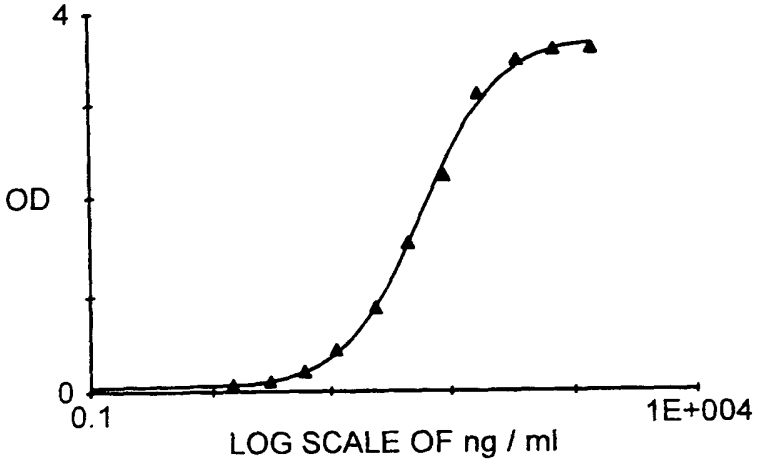
A               S  C  S  V  M  H  E  A  L  H  N  H  Y  T  Q  K  S  L  S  L  -

                TCTCCGGGTAAATGA
         1321   ---------+-----  1335
                AGAGGCCCATTTACT

A               S  P  G  K  *  -
```

FIG. 4 CONT'D

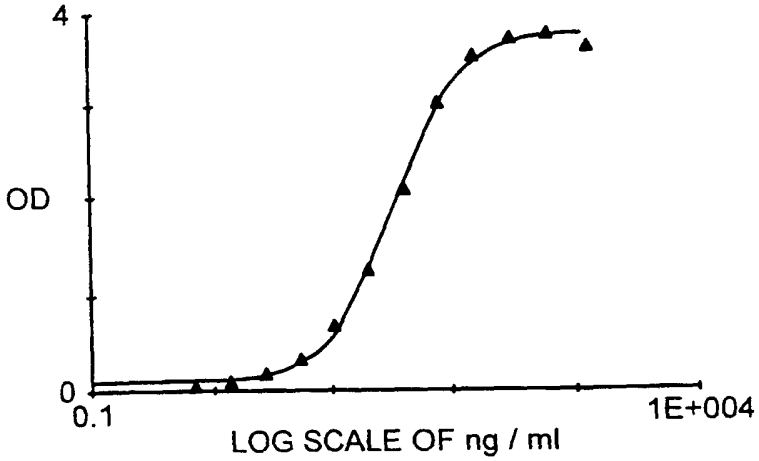
y=(A-D)/(1+(x/C)^B)+D
A=0.0501 B=1.31 C=60.3 D=3.74



CHIMERIC CD23 IgG1m
HALF MAXIMUM BINDING=16.28ng/ml

FIG. 5

y=(A-D)/(1+(x/C)^B)+D
A=0.104 B=1.49 C=37.7 D=3.78



HUMANIZED CD23 IgG1m
HALF MAXIMUM BINDING=15.03ng/ml

FIG. 6